Remarks

Claims 21 and 23-34 are pending in this application. Claim 22 is canceled in this paper without prejudice. Applicants confirm their single species election of "fluoxetine or the R or S isomer thereof," as provided by Mr. Ricardo Moran during the phone conversation with the Examiner on August 17, 2005. Applicants note that currently, claims 21 and 23-28 are readable upon the elected single species, and that claims 29-34 are withdrawn from consideration by the Examiner. No new matter has been introduced.

Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

A. The Rejection of Claims Under 35 U.S.C. § 102 Should Be Withdrawn

On pages 3-4 of the Office Action, claims 21 and 23-27 are rejected as allegedly anticipated by U.S. Patent No. 5,712,302 to Young ("the '302 patent"). Applicants respectfully traverse this rejection.

It is well-settled that "[a] claim is anticipated only if each and every element as set for the in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Claim 21 recites, in part, a pharmaceutical composition comprising R(+) ondansetron, substantially free of its S(-) stereoisomer, and at least one other therapeutic agent listed in that claim. However, the '302 patent does not disclose any of the second therapeutic agents listed in claim 21. Consequently, as the '302 patent does not disclose each and every element of claim 21, Applicants respectfully request that the rejection of claim 21 under 35 U.S.C. §102 be withdrawn.

B. The Rejection of Claims Under 35 U.S.C. §103 Should Be Withdrawn

On pages 4-6 of the Office Action, claims 21-28 are rejected as allegedly obvious over WO 92/00103 by Jones ("the '103 publication"), in view of the '302 patent. In particular, it is alleged that the claims are obvious because: 1) the '103 publication discloses a combination of 5-HT_3 antagonist and 5-HT reuptake inhibitor, and racemic ondansetron and fluoxetine are disclosed as a 5-HT_3 antagonist and a 5-HT reuptake inhibitor, respectively; and 2) the '302 patent discloses that R(+) ondansetron decreases adverse effects associated with racemic ondansetron. Office Action, pages 5-6. Applicants respectfully disagree.

Under current law, a prior art reference or references cannot render a claim obvious unless the PTO provides evidence that the reference or references meet a three-part

test for *prima facie* obvious. To begin with, the prior art reference or references must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant." *See In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000); *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 2005). Where one reference is relied upon by the PTO, there must be a suggestion or motivation to modify the teachings of that reference. *See In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316-17. Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *See WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355, 51 U.S.P.Q.2d 1385, 1397 (Fed. Cir. 1999); *Princeton Biochemicals, Inc.*, 2005 WL 1355127, at *4, 75 U.S.P.Q.2d at 1054; *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002). Second, the prior art references cited by the PTO must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *See In re Dow Chemical* , 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988); *Boehringer Ingelheim Vetmedica, Inc.*, 320 F.3d 1339, 1354, 65 U.S.P.Q.2d 1961, 1971 (Fed. Cir. 2003); *Noelle v. Lederman*, 355 F.3d 1343, 1352, 69 U.S.P.Q.2d 1508, 1516 (Fed. Cir. 2004). Further, "[b]oth the suggestion and the reasonable expectation of success 'must be founded in the prior art, not in the applicant's disclosure.'" *Noelle*, 355 F.3d at 1352, 69 U.S.P.Q.2d at 1515-16 (quoting *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991)). Finally, the PTO must show that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *See Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461, 1473, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1569, 39 U.S.P.Q.2d 1321, 1327 (Fed. Cir. 1996). Applicants respectfully submit that these criteria are not met by the references cited by the Examiner.

First, Applicants respectfully point out that while the '103 publication discloses ondansetron and fluoxetine, those of ordinary skill in the art would not have been motivated to specifically select these two agents and use them in a combination. This is because the combination of ondansetron and fluoxetine is merely one of numerous possible combinations disclosed in the '103 publication, and the '103 publication discloses nothing whatsoever regarding the desirability of that specific combination.

The '103 publication discloses that various combinations of two or three active agents can allegedly be used. The '103 publication, page 1, lines 15-20. The

combinations are namely: 1) 5-HT_3 antagonist + 5-HT reuptake inhibitor; 2) 5-HT_3 antagonist + 5-HT_1 agonist; 3) 5-HT_1 agonist + 5-HT reuptake inhibitor; and 4) 5-HT_3 antagonist + 5-HT reuptake inhibitor + 5-HT_1 agonist. The '103 publication, page 1, lines 24-27. Therefore, at least four different combinations of three classes of molecules are disclosed in the '103 publication. Considering that the '103 publication discloses numerous species for each of the classes it discloses, literally hundreds of different combinations are purportedly encompassed by the '103 publication. Yet, there is no teaching or suggestion in the '103 publication that the specific combination of ondansetron, much less optically pure R(+) ondansetron, and fluoxetine is particularly desirable.

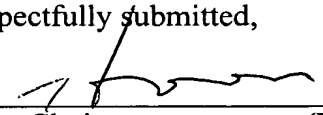
Likewise, the '302 patent, while it may disclose that optically pure R(+) ondansetron may be more advantageous than racemic ondansetron[1], does not teach or suggest anything regarding the desirability of the specific combination of R(+) ondansetron and fluoxetine. Consequently, since none of the cited references provide the motivation required for establishing a *prima facie* case of obviousness, Applicants respectfully submit that the rejection of claims 21-28 under 35 U.S.C. § 103 be withdrawn.

[1] A proposition with which Applicants respectfully disagree. While disclosing that compositions containing R(+) ondansetron "are useful in ameliorating the nausea and vomiting ... while avoiding adverse effects ... associated with the administration of racemic ondansetron," the '302 patent does not teach or suggest that R(+) ondansetron may be used for the treatment of apnea or related disorders as the current specification teaches. The '302 patent, column 1, lines 15-20. Therefore, Applicants point out that the '302 patent's disclosure of the desirability of R(+) ondansetron is in connection with the disorders disclosed therein, and thus, the '302 patent does not provide a general motivation to replace ondansetron with R(+) ondansetron in any and all of its uses.

No fee is believed due for this submission. However, if any fees are required for the entry of this paper or to avoid abandonment of this application, please charge the required fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

Date: January 18, 2006



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